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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/926,385 | 10/24/2001 | Takashi Tojo | 215095US0PCT | 1263 |

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| EXAMINER | |
|---|---|
| LUKTON, DAVID | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/926,385 | TOJO ET AL. | |
| | Examiner | Art Unit | |
| | David Lukton | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-12* is/are rejected.

7)☒ Claim(s) *2-7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' election of Group I is acknowledged, as is the elected specie. Claims 8 and 12 are now rejoined with the elected group.

✧

35 U.S.C §101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture or composition of matter or any new and useful improvement therof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claim 10 is rejected under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

Claim 10 is drawn to a "use" and as such does not fall within a proper statutory class of invention (*Clinical Products v. Brenner* **149** USPQ 475)

✧

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending application Serial No. 10/030161. Although the conflicting claims are not identical, they are not patentably distinct from each other. There is overlap of the claimed genera. [This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented]

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first

patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d)

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses (page 56) that the compound of example 5 inhibits growth of *Candida albicans* FP-633 *in vitro*, and exhibits an MIC of 0.3 *micro*grams/mL. The term "example 5" is somewhat ambiguous, since there is also a "preparation 5" depicted on page 63 of the specification. The assumption, however, is that the compound of "example 5" is contained within the genus defined by the last structure on page 239, wherein "R" is defined on page 240. Accordingly, it is stipulated that the following claim is enabled:

> *A method of inhibiting growth of fungi comprising administering to a human or animal subject in need thereof a compound according to claim 1 for a time and under conditions effective to inhibit growth of said fungi.*

In any case, from this one in vitro experiment, applicants are extrapolating (claim 12) to a method of treating any and all infectious diseases caused by "pathogenic microorganisms". Were the claim limited to treatment of diseases caused solely by fungi, this ground of rejection would be fully justified. But applicants have gone a step further in arguing that any disease caused by any "pathogenic microorganism" can be treated. Microorganisms include bacteria, viruses, and some parasites. There is no evidence that any of these are affected one way or another by the claimed compounds. Returning to the issue of diseases caused by fungi, the reality is that one cannot predict therapeutic success in the treatment of diseases caused by fungi based solely on the finding that fungal growth can be inhibited in a petri dish.

Claim 12 is rejected, since the term "pharmaceutical" implies an assertion of therapeutic efficacy, which is not in evidence. Claim 10 is rejected, since it recites that a "medicament" can be manufactured. A "medicament" is viewed as similar in implied assertion to a "pharmaceutical composition".

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988), the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or

unpredictability of the art, and breadth of the claims. Consider the following references:

- Buchta, V. (*Mycoses* **44** (11-12) 505-12, 2001) discloses that a patient died from a fungal infection despite being treated with compounds that exhibit anti-fungal activity *in vitro*.

- Adam (*Medicine* **65**, 203, 1986) discloses (page 208, col 2) that *in vitro* susceptibility to antifungal agents did not correlate with therapeutic efficacy of the agents.

- Nagasawa M. (*Journal of Infection* **44** (3) 198-201, 2002) discloses that a patient died from a fungal infection despite being treated with compounds that exhibit anti-fungal activity *in vitro*.

- Manfredi R (*Mycopathologia* **148** (2) 73-8, 1999) discloses that two patients died from a cyrotpococcus infection despite being treated with an agent that exhibited anti-fungal activity *in vitro*.

- Wang M. X. (*Cornea* **19** (4) 558-60, 2000) discloses that a patient was treated with an agent that exhibited anti-fungal activity *in vitro*, but that despite this, his fungal sclerokeratitis progressed to endophthalmitis.

- Bhalodia M V (*Journal of the Association for Academic Minority Physicians* **9** (4) 69-71, 1998) discloses that a compound that exhibited anti-fungal activity *in vitro* was not effective to treat a candida infection in a patient

- Moore M. L. (*Journal of Perinatology* **21** (6) 399-401, 2001) discloses that a premature infant died from a fungal infection despite being treated with a compound that exhibits anti-fungal activity *in vitro*.

- Berman, Judith (*Nat Rev Genet* **3** (12) 918-30, 2002) discloses that many immunocompromised patients die from *Candida* infections in spite of having received various dosages of compounds which exhibit anti-fungal activity *in vitro*.

- van Duin David (*Antimicrobial Agents and Chemotherapy* **46** (11) 3394-400, 2002) has disclosed an example of a compound which exhibits antifungal activity *in vitro* but not *in vivo*.

- Marr K. A. (*Antimicrobial Agents and Chemotherapy* 45 (1) 52-9, 2001) discloses that a patient developed a fungal infection despite prophylactic treatment with a compound which exhibits antifungal activity *in vitro*.

In accordance with the foregoing, one cannot "predict" therapeutic efficacy on the basis of fungal growth inhibition *in vitro*. Accordingly, "undue experimentation" would be required to practice the claimed invention.

It is suggested that the term "pharmaceutical" be deleted from claim 9. It is also suggested that claims 10-12 be cancelled.

✧

Claims 8, 10, 12 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 10 is indefinite as to the intended process steps.

- Claim 12 recites the phrase "prophylactic treatment of infectious diseases". However, this appears to constitute a contradiction in terms. The term "prophylactic" implies that the agent is administered before any symptoms of the disease occurs. The term "treatment of infectious disease", on the other hand, implies that the agent is administered after symptoms of the disease occurs. So the question is, for the infectious disease specialist who is endeavoring to prophylactically treat a disease, should the agent be administered before the symptoms emerge, or after?

- In claim 8 on page 439, line 18, the term "reducting" is used. Perhaps the term *reducing* is intended instead

- Claim 8 recites various processes for preparing the compound of formula I. The first of these can be found on page 434, line 24+. This process calls for reduction of a

nitrile to the corresponding amine. This process may well succeed for the case of $R^2$ and $R^3$ both representing hydrogen, but it is not clear how applicants intend to prepare a compound of formula I if $R^2$ or $R^3$ is a substituent other than hydrogen.

*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1653